REMARKS/ARGUMENTS

Claims 41-60 are under examination in the application. The Office Action mailed on April 24, 2008, includes the following objections and rejections:

1. Claims 41-60 are rejected on the ground of nonstatutory obviousness-type double patenting.
2. Claims 41-60 are rejected under 35 U.S.C. 112, first paragraph.
3. Claims 41-60 are rejected under 35 U.S.C. 112, second paragraph.
4. Claims 41-60 are rejected under 35 U.S.C. 112, second paragraph.
5. Claims 41-44, 46, 47, 49-54, 56, 57, 59-60 are rejected under 35 U.S.C. 102(b).
6. Claims 45 and 55 are rejected under 35 U.S.C. 103(a).
7. Claims 47 and 57 are rejected under 35 U.S.C. 103(a).
8. Claims 48 and 58 are rejected under 35 U.S.C. 103(a).

The claims have been amended to further define the instant invention and the physical properties of the product of claim 41. The amendments to the claims finds support in paragraph [0056]:

> [0056] Therefore, when fibroblasts are incorporated into collagen type I matrix, as is the case in the construction of the Patch, the initial culture period encourages the attachment (via integrins) of fibroblasts to collagen provided in the process. During the second phase of matrix organization, the fibroblasts are stimulated to: a) synthesize new collagen and excrete it into the extracellular space; b) by secreting lysyl oxidase further cause aggregation (fibril formation) and organization of newly synthesized collagen; and c) act in the same fashion to organize the collagen provided in the process. Fibroblasts also randomly move and redistribute themselves through the matrix attaching and mechanically pulling on the collagen in the process, and producing the integrity of the Patch. The culture process which is used to produce the Patch is therefore of multiphasic benefit.

As stated in paragraph [0056] the fibroblasts randomly move and redistribute themselves through the matrix attaching and mechanically pulling on the collagen in the process, and producing the integrity of the Patch and as such the final product is a random, not aligned along any axis

structure that does not provide mechanical strength to the matrix due to the random orientation as a non uniform, non directional matrix.

Claims 41-60 are rejected on the ground of nonstatutory obviousness-type double patenting.

Claims 41-60 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,599,526. The Examiner states the subject matter claimed in the instant application is disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter.

A terminal disclaimer in compliance with 37 CFR 1.321(c) will be filed upon allowance of the claims to overcome the rejection based on a nonstatutory double patenting ground provided the patent is shown to be conflicting and the patent is shown to be commonly owned with this Application. See 37 CFR 1.130(b).

Claims 41-60 are rejected under 35 U.S.C. 112, first paragraph.

Claims 41-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action states claims 41-60 as amended introduced new matter that was not supported by the specification as originally filed. The recitation of "molecular collagen" in claims 41 and 51 is said to introduce new matter that is not supported by the original specification.

The Applicants assert that the subject matter of the claims are described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, Applicants fail to see the term "molecular collagen" in claim 41. Claim 41 does contain the term collagen molecules, which is supported throughout the specification and does not introduce new matter. The skilled artisan would understand from the claims and the

specification that the inventors, at the time the application was filed, had possession of the claimed invention that includes collagen, i.e., collagen molecules.

> *Ipsis verbis* disclosure is not necessary to satisfy the written description requirement of section 112. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventor had possession of the subject matter in question.

In addition, the Office Action states the specification does not support the term 14 days. The Applicants assert that the subject matter of the claims are described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the term of 14 days would be recognized by one skilled in the relevant art that the Applicants had possession of the claimed invention. In addition, the term is specifically supported in the specification:

> [0011] FIG. 1B shows the prototype Patch after the matrix reorganization process lasting 12 days, and incubation in phosphate buffered saline (PBS, pH 7.4) at 4.degree. C. During the incubation, PBS is changed every 12 hours for 2-3 days. This process kills the cells and washes out all soluble cell debris and factors associated with the culture medium. An approximate indicator that this process is complete is that the prototype Patch loses the pink color and is now colorless. It is noted that the Patch is still substantially translucent.

The specification states that the process lasted 12 days and included an additional incubation of 2-3 days, the sum of 14-15 days. As such, the term specified in claim 51 is supported in the specification as filed. Similarly, other portions of the specification provide support for the 14 day (2-weeks).

> [0068] When the Patch had reached about 60% of its initial size while retaining its thickness, the medium was removed, the PBS (1.times., 20 ml) added, and the Patch was subsequently maintained at 4.degree. C. The PBS was changed every 2-3 days for 1-2 weeks, the PBS was then removed and sterile water added (20 ml). After several changes of sterile water, the Patch was maintained moist at 4.degree. C. until use. All operations were carried out under sterile conditions using sterile reagents. The absence of cellular component was confirmed with neutral red labeling for viable cells and light microscopy.

As a result, the term of 2 weeks or 14 days is fully supported in the specification as filed and one skilled in the relevant art that the inventors, at the time the application was filed, would recognize the Applicants had possession of the claimed invention. As such, Applicants respectfully request withdrawal of the rejection.

Claims 41-60 are rejected under 35 U.S.C. § 112, second paragraph.

Claims 41-60 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Office Action states:

> Claim 51 recites the expression "cell culture conditions" that does not set forth the metes and bounds of the claims. Recourse to the specification does not define the expression in terms of what are the cell culture conditions.

Applicants assert that the skilled artisan clearly recognizes the term "cell culture condition" and the skilled artisan in this art clearly understand what conditions are necessary to culture cells. It is not necessary for the Applicants to disclose details that are within the scope of the knowledge of the skilled artisan. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. See also *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005)("The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge... As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution."). If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient"). Accordingly, it is not necessary for the Applicants to specifically state each and every condition necessary for the skilled artisan to culture cells to comply with 35 U.S.C. § 112, second paragraph, as such knowledge is within the scope of knowledge of the skilled artisan.

In addition, the claim is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the

Applicants regard as the invention. However, 35 U.S.C. § 112, second paragraph, demands only the language to be as precise as the subject matter permits and that claims, read in light of the specification, reasonably apprise those skilled in the art of the utilization and scope of the invention. *Shatterproof Glass Corp. v. Libbey Owens Ford Co.*, 758 F.2d 613, 225 USPQ 634 (Fed. Cir. 1985); MPEP 7173.05(a). As such, Applicants respectfully request withdrawal of the rejection.

Claims 41-60 are rejected under 35 U.S.C. § 112, second paragraph.

Claims 41-60 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. Applicants submit that the claims as amended fully comply with 35 U.S.C. § 112, second. Applicants respectfully request that the rejection be withdrawn.

Claims 41-44, 46, 47, 49-54, 56, 57, 59-60 are rejected under 35 U.S.C. § 102(b).

Claims 41-44, 46, 47, 49-54, 56, 57, 59-60 are rejected under 35 U.S.C. § 102(b) as being anticipated by US 5,700,688, hereafter referred to as Lee. The Office Action takes the position that the claims 41-60 are anticipated by Lee arguing that it discloses a tissue equivalent material formed from collagen Type I and III mixed with human fibroblasts. Applicants respectfully disagree.

Lee does not **identically disclose every element** of the claimed invention. See *Corning Glass Works v. Sumitomo Electric*, 9 USPQ 2d 1962, 1965 (Fed. Cir. 1989). A reference that excludes a claimed element, no matter how insubstantial or obvious, is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983). Specifically, Lee provides a uniform oriented tissue-equivalent that includes living cells and provides a matrix that is oriented collagen and cell matrix. Lee provides components that are

"oriented" into a "uniform oriented tissue-equivalent." Lee provides that the cell and matrix alignment is critical to the physical strength for the use of the uniform oriented tissue-equivalent. To achieve that physical strength, the cells and matrix of Lee must be incubated for at least 28 days before the increase in mechanical strength (see Figures 9, 10, 12). This orientation and alignment of the structure of Lee is seen in Figure 5 of Lee below.

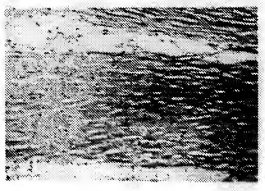


FIG. 5

Figure 5 Lee

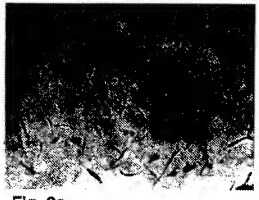
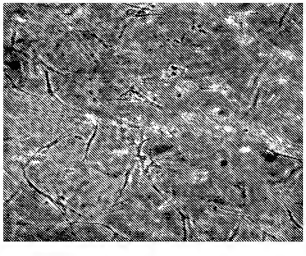


Fig. 2a

Figure 2A, present invention

In Figure 5 of Lee, the alignment of the cells in the matrix is in sharp contrast to the instant invention as seen Figure 2A of the present invention. The cells are not aligned along any axis, nor do they provide mechanical strength to the matrix due to the random orientation. Below is a better image of the three-dimensional, non uniform, non directional matrix formed using of the present invention and provides a structure that is in sharp contrast with the product of Lee.



This figure shows the random cell distribution of the Patch of the present invention. Because the patch is 3-dimensional and the cells are distributed in the matrix in three dimensions and the focus of the microscope objective is in one plane some cells are blurred and are out of focus.

As such, Lee does not disclose an anti-adhesion patch made by the process of mixing Type I collagen molecules with human fibroblast cells that adapt and organize the Type I collagen molecules into monocellular tissue equivalents and whereby the cells organize **randomly** the Type I collagen molecules into the patch in vitro. Lee does not **identically disclose every element** of the claimed invention and cannot anticipate or render obvious the instant invention. Applicants believe that claims 41-60 as amended overcome the rejection based on the art of record. Applicants respectfully request allowance of all the claims.

Claims 45 and 55 are rejected under 35 U.S.C. § 103(a).

Claims 45 and 55 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lee in view of US 6,077,987, hereafter referred to as Breitbart. Applicants respectfully submit that claims 45 and 55 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103(a) for the reasons stated below.

To establish a *prima facie* case of obviousness there must be: (1) some suggestion or motivation either in the reference itself, or within the knowledge generally available to one of ordinary skill in the art, to modify the reference; (2) a reasonable expectation of success, and (3) a teaching or suggestion in the prior art reference of all of the claim limitations (MPEP § 2143). *In re Vacek*, 947 F. 2d. 488 (Fed. Cir. 1991).

The combination fails to establish a *prima facie* case of obviousness. Lee, discussed *supra* and arguments incorporate herein by reference, does not disclose an anti-adhesion patch made by the process of mixing Type I collagen molecules with human fibroblast cells that adapt and organize the Type I collagen molecules into monocellular tissue equivalents and whereby the cells organize randomly the Type I collagen molecules into the patch in vitro. The addition of Breitbart fails to cure these deficiencies. Breitbart does nothing more than teach a method for

enhancing and/or increasing the efficiency of repair of tissues, primarily bone or cartilage, using genetically engineered stem cells. The stem cells of Breitbart fail to supply the missing components to Lee. Furthermore, the genetic manupliation by Breitbart of an entirely different cell line for an entirely different purpose fails to relate to the instant invention. In fact, Breitbart should be held as non-analogous art. The combination fails to teach each and every limitation of the instant invention. As Breitbart is not related to the problem of the instant invention and relates to different cells and different purposes, it is not analogous art and cannot provide a suggestion to modify the reference and fails to provide a reasonable expectation of success. As such, the combination fails on all counts to establish a *prima facie* case of obviousness. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103.

Claims 47 and 57 are rejected under 35 U.S.C. § 103(a).

Claims 47 and 57 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lee in view of US 5,899,936, hereafter referred to as Goldstein. Applicants respectfully submit that claims 47 and 57 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103(a) for the reasons stated below.

To establish a *prima facie* case of obviousness there must be: (1) some suggestion or motivation either in the reference itself, or within the knowledge generally available to one of ordinary skill in the art, to modify the reference; (2) a reasonable expectation of success, and (3) a teaching or suggestion in the prior art reference of all of the claim limitations (MPEP § 2143). *In re Vacek*, 947 F. 2d. 488 (Fed. Cir. 1991).

The combination fails to establish a *prima facie* case of obviousness. Lee, discussed *supra* and arguments incorporate herein by reference, does not disclose an anti-adhesion patch made by the process of mixing Type I collagen molecules with human fibroblast cells that adapt and organize the Type I collagen molecules into monocellular tissue equivalents and whereby the cells organize randomly the Type I collagen molecules into the patch in vitro. The addition of Goldstein fails to cure these deficiencies. Goldstein does nothing more than teach a method for

generating a functional hybrid bioprosthesis of tissue formed naturally of interstitial collagens and treated to kill native cells and remove potentially immunologically active soluble molecules. The combination fails to teach each and every limitation of the instant invention. As Goldstein is not related to the problem of the instant invention but to a tissue replacement, it is not analogous art and cannot provide a suggestion to modify the reference and fails to provide a reasonable expectation of success. As such, the combination fails on all counts to establish a *prima facie* case of obviousness. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103.

Claims 48 and 58 are rejected under 35 U.S.C. § 103(a).

Claims 48 and 58 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US Lee in view of US 5,580,923, hereafter referred to as Yeung. Applicants respectfully submit that claims 48 and 58 are not obvious over the cited art and are, therefore, allowable under 35 U.S.C. § 103(a) for the reasons stated below.

To establish a *prima facie* case of obviousness there must be: (1) some suggestion or motivation either in the reference itself, or within the knowledge generally available to one of ordinary skill in the art, to modify the reference; (2) a reasonable expectation of success, and (3) a teaching or suggestion in the prior art reference of all of the claim limitations (MPEP § 2143). *In re Vacek*, 947 F. 2d. 488 (Fed. Cir. 1991).

The combination fails to establish a *prima facie* case of obviousness. Lee, discussed *supra* and arguments incorporate herein by reference, does not disclose an anti-adhesion patch made by the process of mixing Type I collagen molecules with human fibroblast cells that adapt and organize the Type I collagen molecules into monocellular tissue equivalents and whereby the cells organize randomly the Type I collagen molecules into the patch in vitro. The addition of Yeung fails to cure these deficiencies. Yeung teaches an anti-adhesion films having a substrate materials (such as collagen) and hetero-bifunctional anti-adhesion binding agents, wherein the substrate material is covalently linked to receptive tissue within the body of a patient via the

binding agent. The combination fails to teach each and every limitation of the instant invention, does not provide a suggestion to modify the reference and fails to provide a reasonable expectation of success. As such, the combination fails on all counts to establish a *prima facie* case of obviousness. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 103.

Conclusion

In light of the remarks and arguments presented above, Applicants respectfully submit that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending claims are therefore respectfully requested.

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: October 24, 2008.

Respectfully submitted,

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